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Unhealthy behaviors during pregnancy : who continues to smoke and consume alcohol, and is treatment of anxiety and depressive symptoms effective?

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CHAPTER 1

General introduction

“I started smoking less [during pregnancy] but after several attempts I did not manage to quit. I feel very guilty about this and [I] am afraid that my smoking behavior causes things to go wrong”.

“I worry about my smoking behavior. I want to smoke but I am also afraid to harm my unborn child. This is constantly crossing my mind”.

These are quotes from participants of the Pregnancy Anxiety and Depression (PAD) study. Quitting smoking and alcohol consumption during pregnancy seems self-evident considering the adverse health effects these health behaviors may have on the unborn child. However, not all pregnant women succeed at quitting smoking and alcohol consumption once they know they are pregnant. How do women who do succeed at quitting smoking and alcohol consumption differ from those who do not? What about the period after childbirth; which factors may determine whether women relapse to smoking? And what is the role of anxiety and depressive symptoms with respect to these health behaviors? More importantly, can these symptoms during pregnancy be treated using psychological treatment such as cognitive behavioral therapy?

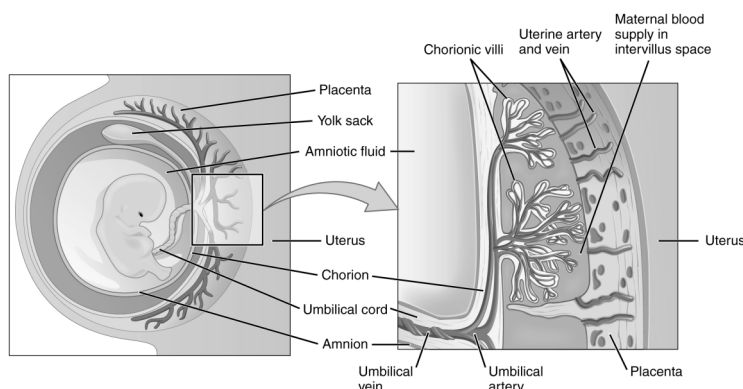
This thesis investigated smoking and alcohol consumption, and the treatment of anxiety and depressive symptoms in the period of pregnancy.

Smoking during pregnancy

Nicotine can pass the placental barrier causing several increased risks for both mother and child (figure 1). Indeed, smoking during pregnancy has been associated with numerous adverse pregnancy outcomes including miscarriage, stillbirth, low birth weight, preterm delivery, placental abruption, changes in brain development and a 150% increase in overall perinatal mortality [1-4]. Smoking during pregnancy has also been associated with problems in the long term such as obesity during adolescence, and behavioral problems and school performance in 5-11 year olds [5,6].

In The Netherlands between 26% and 33% of women of childbearing age smoke, and over the past few years smoking prevalence decreased with almost 10% [7]. Smoking prevalence during pregnancy is estimated to be 13% [8], meaning that between 39% and 50% continues to smoke when expecting. These figures are in accordance with smoking prevalence rates in other industrialized countries [8,9].

Figure 1: Chorionic villi contain the fetus's blood vessels and extend into the wall of the uterus. Maternal and fetal blood cells are not exchanged but separated by the placental barrier/membrane. The placental membrane is however permeable to substances such as nicotine and alcohol. As a result, these substances can enter the blood vessels in the villi, and the umbilical cord, working its way up to the fetus [10].



Alcohol consumption during pregnancy

Just like nicotine, alcohol freely passes the placental barrier and thereby increases the risk of adverse health outcomes for the unborn child. Alcohol consumption during pregnancy has been associated with reduced birth weight, preterm delivery, spontaneous abortion and the fetal alcohol syndrome [11-14]. The fetal alcohol syndrome is characterized by a pattern of abnormalities including growth retardation, and cognitive and behavioral dysfunction, and has been reported when consuming especially large amounts of alcohol frequently [15]. Studies investigating the effects of small to moderate amounts of alcohol show a lack in consensus regarding the negative effects of prenatal alcohol consumption [16]. Nevertheless, pregnant women in The Netherlands and other Western countries are typically advised to abstain completely from alcohol consumption throughout their pregnancy [17-19].

About 80% of women of childbearing age in The Netherlands consume alcohol [7]. Prenatal alcohol consumption prevalence rates for The Netherlands are estimated to vary between 35% and 50% [17], thus between 44% and 63% continues alcohol consumption during pregnancy. Other Western countries showed prenatal alcohol consumption estimates varying between 6% and 54% [20-25]. Large differences in the prevalence rates of prenatal alcohol consumption may reflect differences in drinking culture or attitudes towards prenatal alcohol consumption, but may also be due to the study method [26].

Determinants of continued smoking and alcohol consumption

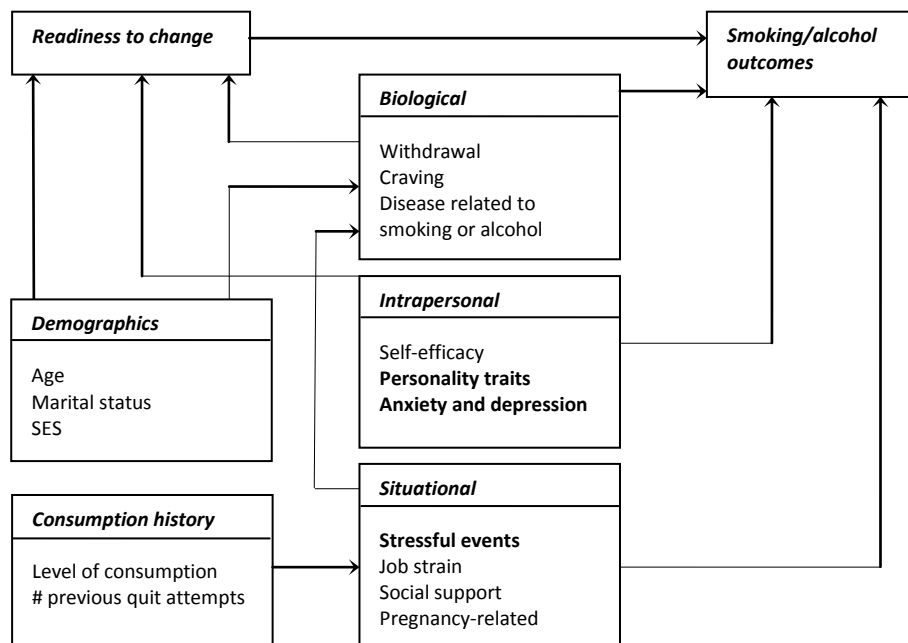
Considering the adverse effects and high prevalence rates of smoking and alcohol consumption during pregnancy, identification of determinants of continued use is important. Increased insight in determinants associated with continued use may support or add to existing healthy lifestyle strategies.

In the general population, several factors have been proposed to be associated with risky health behavior such as smoking and hazardous alcohol consumption. Level of education, level of dependence, social support, cohabiting with a substance using partner and age have all been associated with smoking and alcohol consumption status [27-30]. In addition, personality is considered an important factor with regard to risky health behaviors and may even predict health outcomes later in life [31,32]. For example, higher levels of the personality traits neuroticism and extraversion, and lower levels of conscientiousness have been reported among smokers and alcohol consumers [33-36]. Further, both smoking and alcohol consumption have been identified as a way of coping with psychological stress and negative affect like feelings of anxiety and depression [37-39]. It has been acknowledged that certain events in life can generate psychological stress [40]. Consequently, stressful events may be associated with smoking and alcohol consumption. McKee et al. concluded for example that stressful events were an important risk factor for tobacco use among women, especially events related to health and finance [41]. As for alcohol consumption, Tamers et al. found that women's alcohol consumption increased in the years following marriage or divorce [42].

In pregnancy, women are in general intrinsically motivated to change their health behaviors for the health of their unborn child [43]. In addition, women are extrinsically driven to quit risky health behaviors. For example, women have the desire to behave in a socially acceptable way and are influenced by other's opinions, especially those of friends and family [44]. Despite the motivation to quit smoking and alcohol consumption, there are numerous factors that increase the risk of continued smoking and alcohol consumption during pregnancy. Previous studies found that the level of education, being single, being multiparae, a higher age, exposure to violence or abuse, emotional symptoms (anxiety and/or depressive symptoms), personality traits, pre-pregnancy consumption levels, and high perceived psychological stress are associated with continued smoking and alcohol consumption [26,45,46]. It seems that these factors may be similar to factors reported in the general population at least to some extent.

The bio-behavioral model of smoking cessation and relapse [47], and its adapted version [48], links determinants of smoking outcome in the general population with readiness to change. We proposed to extend this model to alcohol outcomes and the period of pregnancy (figure 2). As a result, this model was used to derive hypotheses on determinants of continued smoking and alcohol consumption during pregnancy.

Figure 2: Factors proposed to be associated with continued smoking and alcohol consumption during and after pregnancy, based on the biobehavioral model of smoking cessation and relapse [47] and the adapted model by van Loon et al. [48].



In this thesis, we focused on intrapersonal and situational factors. Stressful events and personality traits in relation to continued smoking and alcohol consumption during pregnancy were further investigated. Moreover, symptoms of anxiety and depression during pregnancy were taken into account when studying the associations. In the investigation of continued

smoking and alcohol consumption, women who quit smoking or alcohol consumption after learning about their pregnancy were used as a reference group.

Stressful events

Stressful events constitute of a range of, often, adverse experiences. They can, for example, be work related (e.g. losing your job), family related (e.g. having a conflict with your parents), abuse related (e.g. domestic violence) or crime related (e.g. having your house burgled). As noted before, stressful events may be significant sources of psychological stress [40] and consequently, smoking and alcohol consumption may be used as coping mechanisms, also during pregnancy. In the present thesis we investigated stressful events that occurred during pregnancy, including pregnancy-specific stressful events. Pregnancy-specific events are experiences that are related to pregnancy itself, for example finding out about congenital anomalies or experiencing obstetric problems such as vaginal bleeding. So far, only one study investigated the association between general stressful events and continued smoking compared to quit smoking during pregnancy, and did not find an association [49]. This latter study did not take severity of stressful events into account, neither were different categories of events distinguished. To our knowledge, no study on the association between stressful events and continued alcohol consumption has been published to date.

Severity of stressful events can be assessed using three different approaches: a subjective, normative, and contextual approach including an interview to assess the context of the event that has occurred [50]. In this thesis we will focus on the first two approaches only. The subjective approach assesses the severity of the event solely experienced by the respondent. This approach may induce large variations in the appraisal of event severity as respondents may appraise the same event in a different way [51]. The normative approach deals with this response-tendency by assigning a priori a severity score to the events, for example by using the mean score provided by a large sample of individuals [50,52]. As a result, using the normative approach may increase comparability of severity scores between respondents.

Personality

Personality can be described as stable, individual differences in thinking, feeling, and behaving. Personality develops early in life and appears relatively stable throughout life [53]. Changes in personality have been associated with age and major life events (e.g. unemployment, death of a family member) [54]. Pregnancy may be considered as a major life event, although we are unaware of published studies that report on personality changes during pregnancy or as a result of being pregnant. However, previous research does show that personality may change

as a result of birth of a child (decrease in conscientiousness, increase in emotionality) [54,55]. So, it may be that personality remains stable during pregnancy until childbirth.

The well-known Five Factor Model describes personality as consisting of five domains or traits that describe individual differences between people [56]. Each trait can be further divided into six facets (table 1). As described before, in the general population personality traits are associated with smoking and alcohol consumption. Also during pregnancy personality may influence continued smoking and alcohol consumption. Surprisingly, only one study investigated personality traits and continued versus quit smoking, and found that low levels of agreeableness were associated with continued smoking [57]. No study investigating personality and continued versus quit alcohol consumption during pregnancy has been undertaken to date.

Table 1: Five personality traits and their facets

Neuroticism	Extraversion	Openness to experience	Conscientiousness	Agreeableness
Anxiety	Warmth	Fantasy	Competence	Trust
Anger	Gregariousness	Esthetics	Order	Straight-forwardness
Depression	Assertiveness	Feelings	Dutifulness	Altruism
Self-consciousness	Activity	Action	Achievement striving	Compliance
Impulsiveness	Excitement-seeking	Ideas	Self-discipline	Modesty
vulnerability	Positive emotions	Values	Deliberation	Tender-mindedness

Determinants of smoking relapse after childbirth

Although a substantial number of women quit smoking during pregnancy, abstinence does not seem to persist after pregnancy. In The Netherlands it is estimated that up to 62% of women who quit smoking during or before pregnancy start smoking again after childbirth [58]. In other industrialized countries it has also been shown that between 24% and 60% of women who quit smoking during pregnancy relapse after childbirth [59-61]. Preventing postpartum smoking relapse may be beneficial for both the health of the mother and that of other household members, including the newborn. Besides, preventing smoking relapse may be favorable for subsequent pregnancies [62]. Understanding of factors associated with postpartum smoking relapse is required to increase the percentage of abstainers and to add to existing anti-smoking strategies focused on continued abstinence.

To date, evidence suggests that smoking relapse after childbirth is associated with a younger age, a lower educational level, exposure to other smokers, pregnancy-related factors (e.g. unhappy with pregnancy, not breastfeeding, being multiparous), stressful events, depressive symptoms and psychological stress [59,60,63-66]. The depicted model in figure 2 may also be applicable for the period after pregnancy to some extent.

In this thesis we focused on situational factors, i.e. stressful events, and investigated the associations of adverse pregnancy and neonatal outcomes (APDO), as well as transfer from home-delivery to hospital-delivery with postpartum smoking relapse. We assumed that the experience of APDO and transfer to a hospital-delivery may cause psychological stress and consequently trigger smoking relapse. For example, it has been shown that an emergency cesarean section or instrumental delivery is experienced as more stressful compared to a normal vaginal delivery [67,68]. Moreover, these adverse pregnancy outcomes have even been associated with posttraumatic stress [69]. Other APDO such as preterm delivery, low birth weight, or preeclampsia also are stressful for the mother [70,71]. Postpartum depressive symptoms have shown to follow APDO, and may cause postpartum smoking relapse [64,72]. Therefore, we took these symptoms into account as a possible 'mechanistic explanation'. We included a range of APDO of the following categories: adverse antenatal conditions, adverse delivery outcomes, adverse afterbirth outcomes, and adverse neonatal outcomes. To date, the associations of APDO and transfer to a hospital-delivery with postpartum smoking relapse have not been studied before.

Anxiety and depressive symptoms

About 10-20% of all pregnant women experience anxiety and/or depressive symptoms and these symptoms may continue after pregnancy [73,74]. Symptoms of anxiety and depression during pregnancy may include feelings of hopelessness, guilt, a sense of worthlessness, and excessive worries whether or not related to pregnancy itself. Anxiety and depressive symptoms during pregnancy have been associated with a range of adverse maternal and child outcomes. For example, use of tobacco and alcohol, increased risk of suicide, adverse obstetric outcomes (e.g. low birth weight, prematurity), difficulties in mother-child attachment, and emotional and behavioral problems in the offspring have been reported [75,76].

Treatment of anxiety and depressive symptoms during pregnancy may include psychological or psychopharmacological treatment (e.g. antidepressants). Overall, women tend to prefer psychological treatment over antidepressants [77]. Moreover, safety of antidepressant use

during pregnancy remains unclear [78,79]. In the general population, cognitive behavioral therapy (CBT) seems effective in treating anxiety and depression with reported effect sizes of 0.4 or higher [80,81]. It is important to investigate whether this also holds for treatment of anxiety and depressive symptoms during pregnancy. So far, two randomized controlled trials have investigated the effect of CBT on depressive symptoms during pregnancy [82,83], and another randomized controlled trial included both anxiety and depressive symptoms during pregnancy [84]. The latter study did not find CBT to be effective while the other two studies did. However, one of these studies focused on a specific population (Latinas) [83] and the other study was a pilot study including a small number of participants ($n=36$), and was unable to show a statistically significant effect [82]. Clearly, more evidence is needed on the effectiveness of CBT during pregnancy. In this thesis the effectiveness of a CBT intervention was investigated among pregnant women with subclinical anxiety and depression symptoms and disorders. The intervention has been created specifically for pregnant anxious and depressed women. The treatment encompassed several optional modules with specific evidence-based CBT interventions focused on the treatment of anxiety disorders, depressive disorders, trauma and post traumatic stress disorder. In addition, the treatment was targeted at identifying and changing dysfunctional cognitions, coping styles and schemata (cognitive frameworks that help to organize and interpret information).

PAD study and PROMISES study

We used data from the Pregnancy Anxiety and Depression (PAD) and PRenancy Outcomes after a Maternity Intervention for Stressful EmotionS (PROMISES) study [85]. Originally, the PAD study was designed to screen women for eligibility of the PROMISES study.

The PAD study is an ongoing population-based observational prospective cohort study that investigates psychological, medical and social factors during pregnancy and the postnatal period. Women in their first trimester of pregnancy are invited to participate when visiting participating primary midwifery practices and obstetric and gynecology departments of hospitals throughout The Netherlands, or through advertisements in nation-wide media. Women not mastering the Dutch language are excluded. Before entering the study, women provide written informed consent which includes the option to give researchers permission to request for medical birth records. Participants are asked to complete online questionnaires at 14, 19, 24 and 36 weeks of gestation and at 6 and 24 weeks after pregnancy. At present, over 7,500 pregnant women have been included in the PAD study.

Participants of the PAD study showing at least moderate symptoms of anxiety and/or depression are invited to participate in the PROMISES study. This study is a randomized controlled single-blind trial that examines the effects of cognitive behavioral therapy in 300 pregnant women, as compared with care as usual. Outcome measures include behavioral and emotional problems in the offspring, and changes in the level of anxiety and depressive symptoms of the mother. Enrolment of participants follows the same procedures as with the PAD study but additional exclusion criteria apply. These include: currently receiving psychotherapy, having a high suicidal risk, having a substantial physical disease, presenting with illegal substance abuse, and having a psychiatric history on bipolar disorder, psychoses or manic disorder. In addition to the assessments of the PAD study, participants complete questionnaires when the child is 12 and 18 months of age, and child outcomes at 18 months of age are assessed. Furthermore, a diagnostic interview is taken, the SCID-II interview [86].

Detailed information about the design of these studies and measures is described further on in this thesis.

Outline and scope of the thesis

Part of this thesis focused on identifying differences between women who continue smoking and alcohol consumption during pregnancy and those who quit. Furthermore, we studied smoking relapse in the postpartum period. Last, we investigated whether an intervention during the period of pregnancy, cognitive behavioral therapy, would be able to decrease the level of anxiety and depressive symptoms, when compared to care as usual.

Chapter 2 presents the associations of severity of stressful events with continued smoking and continued alcohol consumption during mid-pregnancy. We categorized stressful events according to their characteristics including pregnancy-specific stressful events. In addition, we explored whether anxiety or depressive symptoms could explain part of the associations. We hypothesized that increased severity of stressful events would increase the risk of continued smoking and alcohol consumption. In addition, we assumed that with increasing severity of stressful events the amount of smoking and alcohol consumption among continued users would be higher.

Chapter 3 describes the associations of personality traits with continued smoking and continued alcohol consumption during mid-pregnancy. The Five Factor Model is used to

describe personality traits. Furthermore we explored whether anxiety or depressive symptoms could explain part of the associations. In addition, we explored whether personality traits would be associated with the amount of smoking and alcohol consumption among continued users. Based on previous research and the characteristics of the personality traits, we hypothesized that continued smoking and alcohol consumption would be associated with higher levels of neuroticism and extraversion, and lower levels of conscientiousness, openness to experience and agreeableness.

Chapter 4 presents the associations of adverse pregnancy and neonatal outcomes and transfer from home-delivery to hospital delivery with smoking relapse at six months postpartum. We explored whether postpartum depressive symptoms could explain the associations. We hypothesized that participants who experienced adverse pregnancy and neonatal outcomes and transfer would have an increased risk of smoking relapse.

Chapter 5 describes the design of the PROMISES study, based on the published protocol [87]. In addition, the screening of participants in the PAD study for eligibility for participation in the PROMISES study is discussed.

Chapter 6 reports the effects of cognitive behavioral therapy on the level of anxiety and depressive symptoms at 36 weeks of gestation, as compared to care as usual. We assumed a (greater) reduction in anxiety and depressive symptoms in participants who received cognitive behavioral therapy, compared to participants who received care as usual.

Chapter 7 provides the general discussion of the thesis and gives recommendations for clinical practice and future research.

The thesis ends with a summary in English and Dutch, respectively.

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